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"A STUDY ON PREVALENCE OF ELEVATED HsCRP IN ACUTE VASCULAR EVENTS"

General Medicine

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ABSTRACT

BACKGROUND: Inflammation is a known factor in the development of atherosclerosis and subsequent CVD events. Ongoing inflammation increases the vulnerability of an atherosclerotic lesion to erosion or rupture. The most extensively studied biomarker of inflammation is C-reactive protein (CRP) potentially linked to underlying atherosclerosis. For which standardized high-sensitivity assays (hs- CRP) are widely available which can detect CRP with a sensitivity range of 0.01 to 10 mg/ L. CRP is an acute phase protein that is produced predominantly by liver under the influence of cytokines such as interleukin (IL)-6 and tumor necrosis factor-alpha [1].

METHODS: A study that aimed to analyze levels of hsCRP in determining morbidity and mortality in acute vascular events like Myocardial infarction (MI), unstable angina and stroke in 50 cases comparing to 50 controls with non vascular acute events. A total of 50 patients were enrolled for the study from the in-patient clinics of the Department of General Medicine and Department of cardiology. A single center matched case - control study design was chosen. Age and sex matched controls (50) were also studied for comparison and meaningful interpretation of data.

RESULTS & CONCLUSION: There is definite association of hsCRP in acute vascular events than other non vascular conditions, Very high prevalence of elevated hsCRP with acute vascular events.

Level of hsCRP has no definite role in determining the mortality in patients with acute vascular events.

KEYWORDS:

HsCRP, Myocardial infarction, unstable angina, ischemic stroke

INTRODUCTION:

C-reactive protein: A person's baseline level of inflammation, as assessed by the plasma

concentration of CRP predicts the long-term risk of a first MI [2], ischemic stroke, or peripheral artery disease [3]. Measurement of CRP levels improves risk stratification [4]. Several professional societies have issued statements or guidelines suggesting a role for the measurement of high sensitivity CRP in patients at intermediate risk for coronary heart disease, in whom measurement may help to direct further evaluation and therapy for primary prevention [5].

CRP is a member of the pentraxin family of proteins. It is an acute phase reactant synthesized mainly by the liver. Serum CRP levels are elevated in response to acute infections, inflammatory conditions and trauma. In these clinical situations, the serum CRP levels rise rapidly generally beyond 10mg/l with a concomitant elevation of erythrocyte sedimentation rate {ESR}. [6]

CRP has a relatively long half ife of 18-20h, owing toits stable pentraxin structure. CRP levels do not exhibit diurnal variations inrelation to food intake.High-sensitivity enzyme-linked immunosorbent assay (ELISA) and resonant acoustic profiling (RAP) can detect CRP with a sensitivity range of 0.01 to 10 mg/ l [7]. The hsCRP assays have been standardized across several commercial platforms and can be accurately measured from fresh or frozen plasma [8]. The hsCRP is the most widely evaluated biomarker in the quest for an ideal biomarker for global cardiovascular disease (CVD) risk prediction.

PATHOGENIC ROLE OF CRP —

The participation of inflammatory cells and mediators in atherogenesis and plaque rupture is well established .

The following suggest that there may be a direct effect:

- CRP has been found in atherosclerotic lesions.
- CRP binds to low density lipoprotein (LDL), allowing LDL to be taken up by macrophages without the need for modification [9].
- CRP induces adhesion molecule expression and the production of IL-6 and monocyte chemoattractant protein-1 (MCP-1) in human endothelial cells; these effects might enhance a local inflammatory response within the atherosclerotic plaque by the recruitment of monocytes and lymphocytes [10].

In addition to potentially promoting atherosclerosis, CRP may also have an adverse effect in myocardial infarction that may be mediated in part by an interaction with complement [11].

The value that constitutes an elevation in serum hs-CRP is not clearly defined. A statement from the Centers for Disease Control and Prevention and the American Heart Association (CDC/AHA) reached the following conclusions for the use of serum hs-CRP to estimate cardiovascular risk .

For the determination of cardiovascular risk, values were defined as, hs-CRP levels

- <1 mg/L Low risk,
- 1 to 3 mg/L Intermediate risk,
- >3 mg/L High risk

It was suggested that a value above 10 mg/L should initiate a search for a source of infection or inflammation and the measurement of hs-CRP should be repeated in two weeks.

Among apparently healthy men, the plasma concentration of CRP predicts the long-term risk of a first myocardial infarction, ischemic stroke, hypertension, peripheral vascular disease, sudden cardiac death, and total mortality.

AIMS AND OBJECTIVES

1. To determine the PREVALENCE OF ELEVATED HSCRP IN 50 PATIENTS WITH ACUTE VASCULAR EVENTS.
2. To compare with 50 controls of non vascular acute events.
3. To determine role of hsCRP indetermining the morbidity and mortality.
4. To analyze the levels of hsCRP in patient without any other specific CVS risk factors.

MATERIALS AND METHODS :

STUDY POPULATION

A total of 50 patients were enrolled for the study from the inpatient wards of the Department of General Medicine and Department of cardiology.

Patients who are selected for the study satisfied all the inclusion and exclusion criteria. Written consent was obtained from all patients participating in the study.

Age and sex matched controls (50) were also studied for comparison and meaningful interpretation of data. The controls were recruited from other acute cases that were recruited from the wards; appropriate controls were recruited from the wards. All patients and controls were not from a single ethnic background.

STUDY DURATION
This study was conducted for a period of eighteen months from January 2015 to September 2016.

STUDY DESIGN
A single center matched case- control study design was chosen.

METHODS
Detailed clinical history was taken from each patients and a complete review of their case notes performed.
A complete clinical examination of the nervous system and cardiovascular system was done for each patient.

LABORATORY METHODS
To all selected patients, following investigations were taken.

- ECG
- ECHO
- CPK MB
- CT BRAIN
- FBS
- FLP
- hsCRP
- Other relevant investigations

HsCRP measured after admission in hospital within 1st 24hrs hsCRP were estimated by VITROS 5, 1 FS chemistry system and VITROS 5600 integrated system to quantitatively measure CRP in human serum or plasma.

INCLUSION CRITERIA
FOR CASES
1. Age more than 15 years.
2. Acute myocardial infarction {Evidenced by ECG, elevated CK MB, or ECHO}
3. Ischemic stroke {Two CT BRAIN taken at least 3 days gap showing signs of ischemia}
4. Unstable angina { Evidenced by ECG or elevated CK MB }

FOR CONTROL
1. Age more than15 less than 60.
2. Presence of any illness
3. Event should be acute
4. No cardiovascular risk factors

EXCLUSION CRITERIA
1. Age less than 15 and more than 60
2. Smoking
3. Alcoholism
4. Patient with previous attacks
5. Other inflammatory conditions

a. SLE
b. Scleroderma
c. Rheumatoid arthritis
d. Other Connective Tissue Disorders

6. Immuno suppressant therapy

7. Patient last followup

STATISTICAL ANALYSIS
The significance of difference between two proportions was indicated by the chi-square (**2**) statistic.

The significance of difference in mean between two groups was calculated by Fisher exact test. Variables were considered to be significant if (P<0.05).

RESULTS:
In our study 50 patients were selected and 50 control were selected to analyze for the following

To determine the PREVALENCE OF ELEVATED hsCRP in PATIENTS WITH ACUTE VASCULAR EVENTS.
- To compare with 50 controls of non vascular acute events.
- To determine role of hsCRP in determining the morbidity and mortality.
- To analyze the levels of hsCRP in patients without any other specific CVS risk factors

ACCORDING TO VARIOUS REFERENCES QUOTED ABOVE, THE LEVEL OF hsCRP determines morbidity as well as mortality.

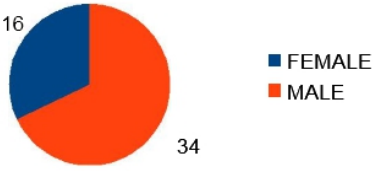
When we divide and analyze as follows
1. With risk factors and elevated hsCRP.
2. Without risk factors only elevated hsCRP.
3. Controls

CONTROLS:

NO OF PATIENTS	DISEASES
15	Fever
5	LRTI
9	Trauma
3	Post operative
9	Diabetic ketoacidosis
3	Acute abdomen
1	pancreatitis
3	UTI
2	gastroenteritis

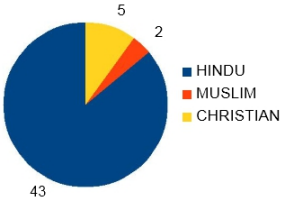
SEX WISE DISTRIBUTION

GENDER	NO OF PATIENTS
MALE	34
FEMALE	16



COMMUNITY WISE DISTRIBUTION

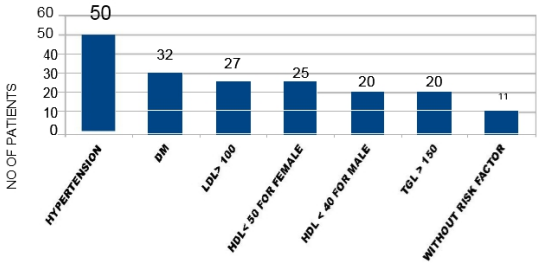
COMMUNITY	NO OF PATIENTS
HINDU	43
MUSLIM	2
CHRISTIAN	5



RISK FACTOR WISE DISTRIBUTION:

TOTAL NO OF PATIENTS	50
HYPERTENSION	32
DIABETES	27
LDL>100	25
HDL <50 FOR FEMALE	20
<40 FOR MALE	
TGL > 150	20
WITHOUT RISK FACTOR	11

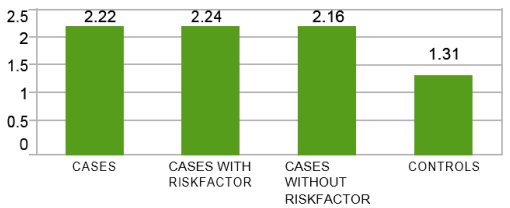
RISK FACTOR DISTRIBUTION



AVERAGE ELEVATED CRP:

NORMAL	CASES	CASES WITH RISK FACTOR	CASES WITHOUT RISK FACTOR	CONTROLS
<0.3	2.22	2.24	2.16	1.31

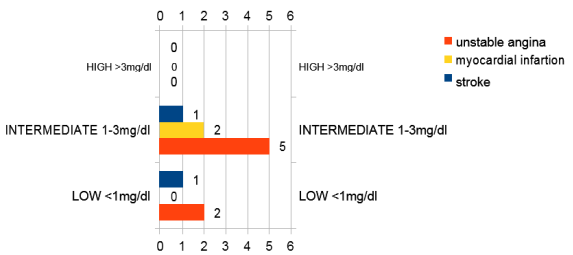
AVERAGE ELEVATED CRP



CLASS WISE DISTRIBUTION WITHOUT RIK FACTORS

TYPE OF DISEASE	LOW <1MG/L	INTERMEDIATE 1-3 MG/L	HIGH 3 MG/L	TOTAL
MYOCARDIAL INFARCTION	0	2	0	2
UNSTABLE ANGINA	2	5	0	7
STROKE	1	1	0	2

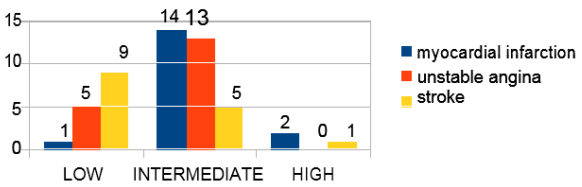
CLASS WISE DISTRIBUTION WITHOUT RISK FACTORS



CLASS WISE DISTRIBUTION FOR ALL CASES

TYPE OF DISEASE	LOW	INTERMEDIATE	HIGH	TOTAL
MYOCARDIAL INFARCTION	1	14	2	17
INFARCTION				
UNSTABLE ANGINA	5	13	0	18
ANGINA				
STROKE	9	5	1	15

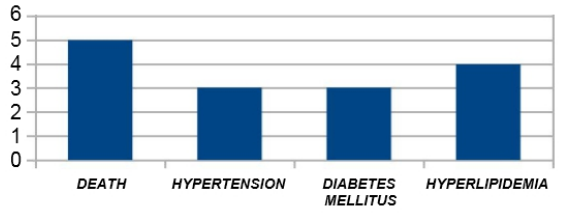
CLASS WISE DISTRIBUTION FOR ALL CASES



MORTALITY AND ASSOCIATED RISK FACTORS

TYPE	NO OF PATIENTS
DEATH	5
HYPERTENSION	3
DIABETES MELLITUS	3
HYPERLIPIDEMIA	4

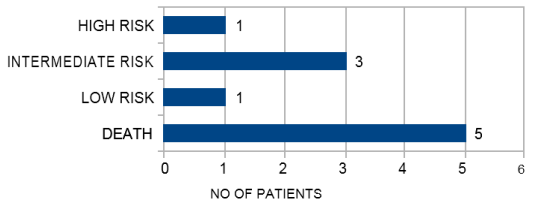
MORTALITY AND ASSOCIATED RISK FACTORS



TOTAL MORTALITY

RISK	NO OF PATIENTS
DEATH	5
LOW RISK	1
INTERMEDIATE RISK	3
HIGH RISK	1

TOTAL MORTALITY



In this study, it is found that:

The prevalence of elevated Hs CRP in selected cases >0.3mg/L - 42/50 84%

Prevalence of elevated Hs CRP in control >0.3mg/L - 32/50 64%

Prevalence of elevated hsCRP in Cases and Controls

	Elevated hsCRP	Normal Level hs CRP	TOTAL
CASES	42	8	50
CONTROL	32	18	50

In considering the statistical significance, used Chi-square test and the result was obtained as follows:

According to Chi-square formula,

X2 = 5.1975 , Degree of freedom = 1

The P value is 0.022619

According to the above results, the P.value is <0.05. So, this signifies that hsCRP has a definitive role in the cardiovascular pathology.

While comparing for patients with risk factors and without risk factors, we have used Fisher exact test and the results are obtained as follows.

Cases with and without risk factors

RISK FACTORS	ELEVATED	NOT ELEVATED
Cases with risk factors	32	7
Cases without risk factors	10	1

The two tailed P value is 0.6658 The P value is >0.05. So, this shows that there is no statistical difference between prevalence of elevated hsCRP in cases with and without risk factors.

While analyzing the significance of mortality, we used the Fisher exact test and the results are obtained as follows

Mortality in Cases with elevated hsCRP

	ELEVATED	NOT ELEVATED
DEAD	5	0
ALIVE	37	8

In considering the statistical significance, used the fisher exact test and the result obtained is as follows The two tailed P value is 0.5774

The P value is >0.05. So this shows no statistical significance.

Therefore the level of hsCRP has no definite role in determining the mortality.

DISCUSSION:

In our study, 16 females were selected, one third of study population. Moreover, included 10% of minority ethnics in our study and the study shows there is no significant variation with community. In our study there is no significant difference in morbidity and mortality between males and females.

In our study 35 persons have underlying cardiovascular risk factors. 18 patients have family history of cardiovascular events. 10 patients have no risk factors, but have elevated CRP.

The average elevated level of CRP in cases with risk factors and without risk factors are significantly above level of controls selected.

Regarding the distribution of cases without risk factors, seven cases are with intermediate risk value i.e., CRP between1 and 3. Six cases are with low risk value.

Regarding the distribution of cases, thirty two cases are in intermediate risk value, fifteen cases are with low risk value and three patients are in high risk group.

Regarding the total mortality, most of the patients who died i.e. three in number belong to intermediate risk category, one person with low risk and one person with high risk.

On comparing the mortality in patients with various risk factors, hyperlipidemia plays a major role i.e. nearly four of the five deaths. Hypertension and diabetes are second most leading comorbid condition.

The study clearly shows hsCRP has a definite role in cardiovascular morbidity and mortality.

Studies with clinical CVD events included a case-control study by Rajeshwar et al [12] (1,156 subjects; hsCRP levels predict ischaemic stroke), Goswami et al[**13**] (200 subjects; hsCRP is an independent predictor of CAD) and Guruprasad et al[**14**] (442 subjects; hsCRP levels are associated with an increasing severity of CAD).

A prospective cohort study by Rao et al[**15**] with 1,021 subjects, of whom 772 had established CAD and the rest were controls, found that hsCRP was an independent predictor of repeat coronary events.

CONCLUSIONS AND SUMMARY

In this study it is clearly shown that most of patient selected had:

- Very high prevalence of elevated hsCRP with acute vascular events.
- There is definite association of hsCRP in acute vascular events than other non vascular conditions.
- The analysis in patient without any specific cardiovascular risk factors shows definite relative correlations
- Probably hsCRP may play a role in pathogenesis as mentioned in the literature above which needs further studies.
- Level of hsCRP has no definite role in determining the mortality in patients with acute vascular events.

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